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NOTICE OF ALLOWANCE AND FEE(S) DUE

68514 7590 02/02/2010

Don D. Cha
547 Buena Vista Road
Golden, CO 80401

EXAMINER	
MOORE, WILLIAM W	
ART UNIT	PAPER NUMBER
1656	

DATE MAILED: 02/02/2010

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/518,081	03/03/2000	Leland Shapiro	SHAP-000300	5429

TITLE OF INVENTION: METHODS AND COMPOSITIONS FOR INHIBITING APOPTOSIS USING SERINE PROTEASE INHIBITORS

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	YES	$755	$0	$0	$755	05/03/2010

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

A. If the status is the same, pay the TOTAL FEE(S) DUE shown above.

B. If the status above is to be removed, check box 5b on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above, or

If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check box 5a on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and 1/2 the ISSUE FEE shown above.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PTOL-85 (Rev. 08/07) Approved for use through 08/31/2010.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
Commissioner for Patents
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INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

68514 7590 02/02/2010

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547 Buena Vista Road
Golden, CO 80401

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

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09/518,081	03/03/2000	Leland Shapiro	SHAP-000300	5429

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nonprovisional	YES	$755	$0	$0	$755	05/03/2010

EXAMINER	ART UNIT	CLASS-SUBCLASS
MOORE, WILLIAM W	1656	514-021000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

❑ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.

❑ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list

(1) the names of up to 3 registered patent attorneys or agents OR, alternatively,

(2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 _____

2 _____

3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE (B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ❑ Individual ❑ Corporation or other private group entity ❑ Government

4a. The following fee(s) are submitted:

❑ Issue Fee

❑ Publication Fee (No small entity discount permitted)

❑ Advance Order - # of Copies _____

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❑ A check is enclosed.

❑ Payment by credit card. Form PTO-2038 is attached.

❑ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)

❑ a. Applicant claims SMALL ENTITY status. See 37 CFR 1.27.

❑ b. Applicant is no longer claiming SMALL ENTITY status. See 37 CFR 1.27(g)(2).

NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

Authorized Signature _____ Date _____

Typed or printed name _____ Registration No. _____

This collection of information is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

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EXAMINER	
MOORE, WILLIAM W	
ART UNIT	PAPER NUMBER
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Determination of Patent Term Extension under 35 U.S.C. 154 (b)
(application filed after June 7, 1995 but prior to May 29, 2000)

The Patent Term Extension is 0 day(s). Any patent to issue from the above-identified application will include an indication of the 0 day extension on the front page.

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Extension is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (http://pair.uspto.gov).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

Notice of Allowability	Application No.	Applicant(s)	
	09/518,081	SHAPIRO, LELAND	
	Examiner	Art Unit	
	WILLIAM W. MOORE	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *the amendment filed 17 November 2009 and the interview conducted 27 January 2010*.

2. ☒ The allowed claim(s) is/are *33-40 and 42-53*.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☐ Examiner's Amendment/Comment
8. ☐ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

/William W. Moore/
Examiner, Art Unit 1656

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee. All allowed claims are included below, whether or not amended, to assist the printer.

Amend claims 33, 34, 27, 39, 43, 44, 47, and 49 thus:

33. (Previously Presented) A method of treating ~~arthritis,~~ muscular dystrophy, multiple sclerosis, arteriosclerosis, ~~autoimmune disease, ischemia-reperfusion injury,~~ neurodegenerative disease, myocardial infarction, or stroke in a subject in need of such a treatment, said method comprising: inhibiting apoptosis in the subject by administering ~~at least once daily and no more than once hourly~~ a therapeutically effective amount of α_1-antitrypsin, an oxidation-resistant α_1-antitrypsin Met358 variant or a free radical-resistant α_1-antitrypsin M358 variant.

34. (Amended) The method of Claim 33, wherein the effective amount of α_1-antitrypsin, an oxidation-resistant α_1-antitrypsin Met358 variant, or a free radical-resistant α_1-antitrypsin M358 variant is at least 0.001 g/kg body weight and no greater than 1 g/kg ~~70 g/kg~~ body weight.

35. (Previously Presented) The method of Claim 33, further comprising administering at least one free radical scavenger or inhibitor.

36. (Previously Presented) The method of Claim 33, in which the subject is a human.

37. (Amended) The method of Claim 33, in which the therapeutically effective amount is sufficient to provide at least 5 nanograms per milliliter and no greater than 10 milligrams per milliliter ~~10 pM and no greater than 2 mM~~ of the α_1-antitrypsin, an oxidation-resistant α_1-antitrypsin Met358 variant, or a free radical-resistant α_1-antitrypsin M358 variant inhibitor in the biological fluid of the subject.

38. (Previously Presented) The method of Claim 37, in which the biological fluid is blood.

39. (Amended) The method of Claim 37, in which the therapeutically effective amount is sufficient to provide at least 0.5 μM and no greater than 100 μM ~~2000 μM~~ in the biological fluid of the subject.

40. (Previously Presented) The method of Claim 33, in which the administering is parenterally, orally, vaginally, rectally, nasally, buccally, intravenously, intramuscularly, subcutaneously, intrathecally, epidurally, transdermally, intracerebroventricularly, by osmotic pump, by inhalation, or combinations thereof.

42. (Previously Presented) The method of Claim 33, wherein the neurodegenerative disease is Alzheimer's disease or Downs Syndrome.

43. (Currently Amended) A method for treating ~~a arthritis,~~ muscular dystrophy, multiple sclerosis, arteriosclerosis, ~~autoimmune disease, ischemia-reperfusion injury,~~ neurodegenerative disease, myocardial infarction, or stroke in a subject in need of such a treatment, said method comprising administering ~~at least once daily and no more than once hourly~~ to the subject a therapeutically effective amount of α_1-antitrypsin, an oxidation-resistant α_1-antitrypsin Met358 variant or a free radical-resistant α_1-antitrypsin M358 variant.

44. (Amended) The method of Claim 43, wherein the effective amount of α_1-antitrypsin, an oxidation-resistant α_1-antitrypsin Met358 variant, or a free radical-resistant α_1-antitrypsin M358 variant is at least 0.001 g/kg body weight and no greater than 1 g/kg ~~70 g/kg~~ body weight.

45. (Previously Presented) The method of Claim 43, further comprising administering at least one free radical scavenger or inhibitor.

46. (Previously Presented) The method of Claim 43, in which the subject is a human.

47. (Amended) The method of Claim 43, in which the therapeutically effective amount is sufficient to provide at least 5 nanograms per milliliter and no greater than 10 milligrams per milliliter ~~10 pM and no greater than 2 mM~~ of the α_1-antitrypsin, an oxidation-resistant α_1-antitrypsin Met358 variant, or a free radical-resistant α_1-antitrypsin M358 variant inhibitor in the biological fluid of the subject.

48. (Previously Presented) The method of Claim 47, in which the biological fluid is blood.

49. (Amended) The method of Claim 47, in which the therapeutically effective amount is sufficient to provide at least 0.5 μM and no greater than 100 μM ~~2000 μM~~ in the biological fluid of the subject.

50. (Previously Presented) The method of Claim 43, in which the administering is parenterally, orally, vaginally, rectally, nasally, buccally, intravenously, intramuscularly, subcutaneously,

intrathecally, epidurally, transdermally, intracerebroventricularly, by osmotic pump, by inhalation, or combinations thereof.

51. (Previously Presented) The method of Claim 43, wherein the neurodegenerative disease is Alzheimer's disease or Down's Syndrome.

Add the new claims 52 and 53.

52. (New) The method of claim 33, in which the therapeutically effective amount is administered at least once daily and no more than once hourly.

53. (New) The method of claim 43, in which the therapeutically effective amount is administered at least once daily and no more than once hourly.

Authorization for this examiner's amendment was given in a telephone interview with Mr.Don D. Cha on 27 January 2010.

The following is an examiner's statement of reasons for allowance:

Applicant's amendment to the specification, deleting Figure 1 and making the former Figure 2 the Figure 1 of the application, overcomes the objection of record made at pages 4 and 5 of the communication mailed 29 May 2009, and the objection is WITHDRAWN. Claims 33 and 43 are amended above to remove three of the recited medical conditions that are implicated by the prior art cited in the communication mailed 29 May 2009 as well as to remove recitations of a range of schedules for administration of an α_1-antitrypsin inhibitor [AAT] in favor of stating this range in the new claims 52 and 53. Claims 34, 37, 39, 44, 47, and 49 are amended above to more particularly indicate the effective physiological concentrations of the intended subject matter, i.e., treatment with a polypeptide inhibitor, described in disclosures found at page 7, line 17, and lines 23-31, of the specification. Thus claims 33-40 and 42-53 are allowed herewith.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is 571.272.0933 and whose FAX number is 571.273.0933. The examiner can normally be reached Monday through Friday between 9:00AM and 5:30PM EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisory Primary Examiner, Manjuanth Rao, can be reached at 571.272.0939. The official FAX number for all communications for the organization where this application or proceeding is assigned is 571.273.8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571.272.1600.

/William W. Moore/
Examiner, Art Unit 1656

/Nashaat T. Nashed/
Primary Examiner, Art Unit 1656